Diagnostic Criteria and Staging Systems in ALS

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A panel of experts considers the usefulness of diagnostic criteria and disease staging systems for patients with amyotrophic lateral sclerosis (ALS) as entry criteria for clinical trials.

EP. 1: An Overview of Causes and Risk Factors for ALS

EP. 2: Diagnosing ALS: Signs and Symptoms

EP. 3: Diagnosing ALS: Common Mimics

Richard S. Bedlack, MD, PhD, MS: Back to you, Ammar. I hear about these different sets of diagnostic criteria called the El Escorial World Federation of Neurology Criteria and the Awaji Criteria for the Diagnosis of Amyotrophic Lateral Sclerosis [ALS], and I hear about these different staging systems. Can you explain those to us? How useful are those in practice?

Ammar Al-Chalabi, MB, ChB, PhD: You have to separate the 2 things, the diagnostic criteria and the staging systems, even though there is some relationship between them. The diagnostic criteria were initially designed for research purposes for clinical trial entry because the diagnosis needed to be an algorithmic process so you could say, "Yes, all of these people entering this clinical trial have ALS," rather than using the "wisdom" of an ALS specialist, wisdom in inverted commas.

in 1993 or 1994, sometime like that. They divided the regions in the body into 4 parts: bulbar, cervical, thoracic, and lumbar. The rules were that you had to have lower motor neuron findings and upper motor neuron findings in the different body regions, and then by the combination of upper and lower motor neuron findings, you could classify people as to whether they had ALS. It was not a binary, "Yes, you have ALS," or "No, you do not have ALS." It was categorized into parts a bit like how multiple sclerosis was being categorized at the same time: suspected, possible, probable, and definite. That worked for clinical trials. It meant people could say, "We have taken everybody who has more than suspected ALS," or "We have everybody who is in the definite and probable categories."

But it led to a lot of confusion because they were called diagnostic criteria, but really, they were entry criteria for clinical trials. They had these words definite, probable, and possible ALS, even in somebody who the ALS specialist knew this person had ALS, but the person is being told that they have El Escorial-possible ALS. There is a lot of confusion around the nomenclature. It is probable that, if it had been called grade 1, 2, 3, and 4 ALS or something like that, it would have been a better choice. It is easy to make these comments in retrospect. Because of those difficulties and because one of the categories, which was suspected ALS, was pure lower motor neuron involvement, and because sometimes lower motor neuron findings can be difficult to find clinically but they are present electrophysiologically, the criteria were revised in Awaji, Japan.

The Awaji criteria were designed to allow neurophysiological investigation to replace clinical examination as evidence for lower motor neuron involvement in a limb, so you could then change categories. It also allowed fasciculation, which was the key thing, in an unaffected limb.

More recently at the Gold Coast in Australia, Jeremy nicely summarized all the findings from the meeting. We had a big meeting of many ALS specialists, and those criteria were simplified again, but we took on board the lessons of the last 25 years and understood that it is useful having a binary, "Yes, you have ALS," or "No, you do not have ALS." Now there are Gold Coast criteria that are designed around the El Escorial criteria, and they say that you have ALS if you have involvement in these body regions in a particular way. If people are interested, the paper is published. We can go through it. To summarize them briefly, the person must have progressive weakness without sensory involvement and with other causes excluded. The 3 body regions are used: bulbar, upper limbs, and lower limbs. You have to be involved of upper and lower motor neurons in 1 body region if that is what was affected, or lower motor neuron involvement in 2 body regions. That is the summary of the criteria for diagnosis.

As Jeremy said earlier, and as Jinsy has also said, an ALS specialist is the keyway of making the diagnosis rather than criteria, but they are useful for entry into research. In terms of clinical staging, staging is important in

stage of disease. It also allows you to measure whether treatment is improving because you will go back through the stages.

In ALS, there has not been a staging system for a long time. People tried various types, and they did not work, or they did not take hold. More recently, 2 staging systems have come into being. One is the King's ALS clinical staging system, which now widely uses the El Escorial regions of bulbar, upper limb, and lower limb. It counts the number of regions involved. If you have 1 region involved, you have stage 1. If you have 2 regions, then you are in stage 2, and if you have 3 regions, you are in stage 3. If you have the need for nutritional support or respiratory support, and those are defined within the staging system, then you are automatically in stage 4 regardless of the number of regions involved.

Using that system seems to correlate quite well with the disease stage intuitively. If you asked any person dealing with ALS, it does not have to be a specialist, "Do you think this person is early disease, middle disease, or late disease? What number would you give their disease stage?" then it correlates quite well with that algorithm.

There is also a functional staging system called the MiToS [Milano-Torino system], derived from the ALS functional rating scale, which asks questions in 12 different domains about function. There is an algorithm that uses those answers to stage people into 1 of 5 functional stages or the sixth stage, which is death.

Richard S. Bedlack, MD, PhD, MS: Are these things that you would think a primary care doctor, or a general neurologist should know about, or are they more for ALS experts, especially those who do trials?

Ammar Al-Chalabi, MB, ChB, PhD: They are not something that a primary care physician would need to know at all. Even many neurologists would not need to know them. It is for an ALS specialist or for entry into trials.

Richard S. Bedlack, MD, PhD, MS: Thank you for watching this NeurologyLive® Peer Exchange. If you enjoyed the content, please subscribe to our e-newsletters to receive upcoming Peer Exchanges and other great content right in your inbox.

Transcript Edited for Clarity